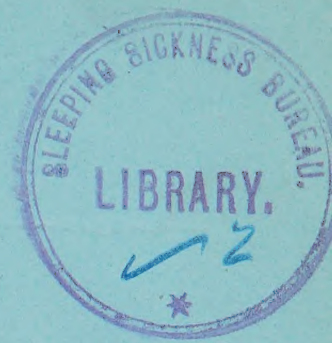


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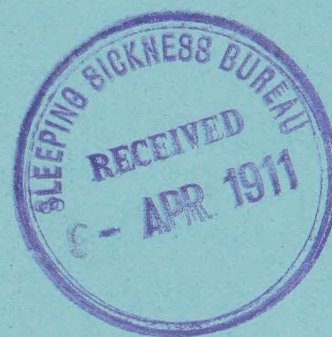
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Experiments to Investigate the Infectivity of Glossina palpalis
Fed on Sleeping Sickness Patients under Treatment.

BY COLONEL SIR DAVID BRUCE, C.B., F.R.S., A.M.S.; AND
CAPTAINS A. E. HAMERTON, D.S.O., AND H. R. BATEMAN,
R.A.M.C. (Sleeping Sickness Commission of the Royal Society,
Uganda, 1908-10); AND DR. R. VAN SOMEREN, Uganda
Medical Staff.

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*Experiments to Investigate the Infectivity of Glossina palpalis
Fed on Sleeping Sickness Patients under Treatment.*

By Colonel Sir DAVID BRUCE, C.B., F.R.S., A.M.S.; Captains A. E. HAMERTON, D.S.O., and H. R. BATEMAN, R.A.M.C. (Sleeping Sickness Commission of the Royal Society Uganda, 1908-10); and Dr. R. VAN SOMEREN, Uganda Medical Staff.

(Received November 23, 1910,—Read February 2, 1911.)

Introduction.

It is well known that there are cases of Sleeping Sickness in man which, under treatment, may enjoy long periods of apparent good health. In these cases the individual is often able to live an active life, and insists on being at liberty to go about as he pleases. In Uganda care is taken to prevent such cases entering the fly-areas; but the difficulty in maintaining a supervision strict enough to check occasional visits to these areas is obviously great, and in other countries may be insuperable, so that the question as to how drug treatment can influence the infectivity of these patients to the fly may be considered to be of importance.

Other points arise from the consideration of this question, viz.:—Can one or more doses of a trypanocidal drug render a Sleeping Sickness patient non-infective to *Glossina palpalis*? Does prolonged treatment during any stage of the disease render cases of Sleeping Sickness innocuous to the fly? If it be proved that the treatment of Sleeping Sickness patients by certain drugs does not prevent them infecting *Glossina palpalis*, then what percentage of cases give a positive result? and what percentage of flies are infected from these cases, as compared with the number of flies infected from untreated cases?

To answer these questions it is necessary to classify under various headings the patients who are the subjects of this paper; to state whether treated or untreated; if the latter, to give details concerning the nature of the treatment, the duration of treatment, and the total quantity of drugs received. The presence or absence of *Trypanosoma gambiense* in the blood or lymph glands of each patient should also be noted.

The classification of patients, according to the stage of the disease in which they present themselves, is that adopted by Dr. A. D. P. Hodges, C.M.G., Principal Medical Officer, Uganda, in the "Progress Report on the Uganda Sleeping Sickness Camps," from December, 1906, to November 30, 1908.

Class A.—Those who are apparently in good health: gland enlargement with trypanosomes present in the glands.

Class B.—Those in whom there are early signs from which the existence of Sleeping Sickness may be reasonably suspected.

*Class C.**—Those in whom clinical signs are well marked.

*Class D.**—Advanced cases.

These experiments were carried out from January to March, 1910. Of the 33 patients under observation,

			6 belonged to Class A.
19	„	„	B.
7	„	„	C.
1	„	„	D.

The methods adopted to test the degree of infectivity of patients to the fly in different stages of the disease were: (1) By mechanical transmission from Sleeping Sickness patient to normal monkey, and (2) by transmission of the disease from Sleeping Sickness patient to normal monkey after the parasite had completed its development in the fly.

1. *By Mechanical Transmission from Sleeping Sickness Patient to Normal Monkey.*

The procedure in testing the first method was as follows:—A cage of laboratory-bred flies was first placed for two minutes upon the bare shoulders of a patient suffering from Sleeping Sickness, which was time enough to allow the majority of the flies to draw some blood, but not enough to satisfy them. After an interval of five minutes the cage was transferred to the abdomen of a normal monkey, where it remained for two minutes, by which time nearly all the flies had completed their feed. This procedure was repeated daily for six days.

Ten of the patients under experiment had been treated with soamin and perchloride of mercury administered by subcutaneous injection. Two patients, who had been under treatment for one year, had received several doses of atoxyl, in addition to soamin and mercury.

Trypanosomes had been found at one time in the glands of all the patients, but no trypanosomes were found in their blood during the time the flies were being fed upon them.

* Classes C and D are not now differentiated.

Table I.—Transmission of *Trypanosoma gambiense* from Sleeping Sickness Patients to Healthy Monkeys by Interrupted Feeding.

No. of experi-ment.	Class of patient.	If treated.	Duration of treatment.	No. of doses.	No. of flies fed.	No. of times flies fed.	Result.
2014	A	Yes	7 days	2	75	6	—
2137	B	"	7 "	2	65	7	—
2144	C	"	7 "	2	75	6	—
2146	B	"	7 "	2	65	6	—
2013	A	"	30 "	4	75	6	—
2027	B	"	30 "	4	75	6	—
2029	B	"	30 "	4	75	6	—
2150	C	"	30 "	4	70	7	—
2152	C	"	30 "	4	50	7	—
2158	B	"	30 "	4	60	6	—
2139	B	"	1 year	?	70	6	—
2154	B	"	1 "	?	50	6	—
2012	B	No	Nil	Nil	75	6	—
2281	B	"	"	"	100	6	—
2284	B	"	"	"	50	6	—

Remarks.—These experiments are all negative—a not unexpected result now that it is known that the mechanical transmission of Sleeping Sickness may be a somewhat rare event in Nature. The question as to whether the medicinal treatment of Sleeping Sickness patients has any preventive influence on this method of transmission remains unanswered. It may, however, be noted that in the two untreated cases, viz., Experiment 2281, Class B, and Experiment 2284, Class B, the disease was not transmitted mechanically, but, as will be seen later (Table III, Experiments 2280 and 2298), was conveyed after a period of development of the parasite within the fly.

2. *By Transmission of the Disease from Sleeping Sickness Patient to Normal Monkey after the Parasite had Completed its Development in the Fly.*

The procedure adopted in the second method for transmitting the disease from a Sleeping Sickness patient to a monkey was as follows:—A cage of laboratory-bred flies was fed daily for five or six days upon a patient suffering from Sleeping Sickness. They were then starved for 48 hours, and subsequently fed daily for 50 days upon a normal monkey.

In most of these experiments the flies were dissected and examined for flagellates after the period of feeding upon the normal monkey. The monkey's blood was subsequently examined twice weekly for one month after the last date on which the flies were fed upon it.

Trypanosomes had been found at one time in the glands of all these patients, but no trypanosomes were found in their blood during the time the flies were being fed upon them.

In the following tables all the details bearing on each class of patient are given :—

Table II.—Transmission of *Trypanosoma gambiense* from Sleeping Sickness Patients, Class A, to Healthy Monkeys, an Interval of Time being allowed for the Development of the Trypanosomes in the Fly.

No. of experiment.	Duration of treatment.	No. of doses.	No. of flies fed on patient.	No. of days flies fed on patient.	No. of days flies fed on monkey.	Result.	Remarks.
1941	7 days	2	125	6	50	—	Monkey remained healthy.
1973	7 „	2	100	6	50	—	„
1969	1 month	4	100	7	50	—	„
1995	1 „	4	130	4	50	—	„
2240	2½ years	?	75	4	50	—	„
2252	2½ „	?	80	4	50	—	„

Remarks.—Reference to Table II will show that six patients in Class A stage of the disease were under treatment. Two of these had been under treatment for one week, and had each received two injections of soamin, 0·01 gramme, combined with perchloride of mercury, 0·02 gramme. Two had been under treatment for one month, and had received four injections of soamin, 0·01 gramme, and perchloride of mercury, 0·02 gramme, per dose. Two cases had been under treatment for two and a-half years: the total quantity of drugs received being, in one case, atoxyl, 16·2 grammes, perchloride of mercury, 2·4 grammes, and orpiment, 8·6 grammes; the other case had received 18·8 grammes of atoxyl, 2·4 grammes of perchloride of mercury, and 8·6 grammes of orpiment.

Sleeping Sickness was not transmitted from any of these patients to monkeys by the flies.

Two hundred and seventy-three flies were dissected between the 4th and 51st days after feeding upon infected patients, but no flies were found infected with flagellates.

Only one patient belonging to Class D was available for these experiments. This patient had been under treatment for one and a-half years, and had been treated with a total quantity of 13·4 grammes atoxyl, 0·4 gramme perchloride of mercury, and 6·5 grammes orpiment.

Flies were not infected from this case, and the disease was therefore not transmitted to a normal monkey.

Table III.—Transmission of *Trypanosoma gambiense* from Sleeping Sickness Patients, Class B, to Healthy Monkeys, an Interval of Time being allowed for the Development of the Trypanosomes in the Fly.

No. of experiment.	Duration of treatment.	No. of doses.	No. of flies fed on patient.	No. of days flies fed on patient.	No. of days flies fed on monkey.	Result.	Remarks.
1993	7 days	2	100	4	50	—	Monkey remained healthy.
2091	7 "	2	50	5	50	—	"
2094	7 "	2	60	5	50	—	"
2170	7 "	2	60	6	50	—	"
1975	30 "	4	100	5	50	—	"
1987	30 "	4	65	5	50	—	"
1991	30 "	4	90	4	50	—	"
2068	30 "	4	65	6	50	—	"
2070	30 "	4	80	6	50	—	"
2107	30 "	4	65	6	50	—	"
2195	30 "	4	50	6	50	—	"
2248	30 "	4	65	4	50	—	"
2096	1 year	8	60	5	50	—	"
2109	1 "	9	65	5	50	—	"
2172	1 "	8	60	5	50	—	"
2193	1 "	9	60	6	50	—	"
2254	2 $\frac{1}{4}$ years	?	80	4	50	—	"
2256	2 $\frac{1}{4}$ "	?	60	4	50	—	"
2258	3 $\frac{1}{2}$ "	?	60	4	50	—	"
1943	Nil	Nil	65	6	50	—	"
1957	"	"	100	4	50	—	"
1967	"	"	110	6	50	—	"
2048	"	"	50	6	50	—	"
2280	"	"	130	4	50	+	<i>T. gambiense</i> appeared in blood.
2298	"	"	80	3	50	+	"

Remarks.—In Table III, Class B, 25 experiments from 19 different patients are recorded. Six of these were from untreated cases.

Sleeping Sickness was transferred from two untreated patients to normal monkeys. The flies belonging to these experiments were not dissected.

The remaining four experiments from untreated cases were negative, both as regards infection of the flies (190 dissected) and the conveyance of the disease to monkeys.

Of the 19 negative experiments from cases under treatment, four were from two patients who had been under treatment for one week. They had each received two injections of soamin in 1-gramme doses, combined with 0·02 gramme of perchloride of mercury. Eight experiments were from patients who had been one month under treatment. They had each received four injections (soamin 1 gramme, and perchloride of mercury 0·02 gramme, per dose). Four experiments were from two cases who had been under treatment for 11 months. One of these had received injections amounting in all to soamin 8 grammes, HgCl₂ 0·10 gramme, and orpiment 2 grammes. The other patient had received a total amount of soamin 9 grammes, HgCl₂ 0·16 gramme, and orpiment (?). Two experiments were from patients who had been under treatment for two and a-quarter years. They had each received a total quantity of drugs amounting to atoxyl 19·7 grammes, HgCl₂ 0·06 gramme, orpiment 4·60 grammes, and soamin 4 grammes. One experiment was from a patient who had been three and a-half years under treatment, and had received during the last 18 months atoxyl 9·5 grammes, soamin 7·5 grammes, and orpiment 4·6 grammes.

From these 19 negative experiments 509 flies were dissected between the 4th and 52nd days after their last infected feed. No flagellates were found in any of them.

Table IV.—Transmission of *Trypanosoma gambiense* from Sleeping Sickness Patients, Class C, to Healthy Monkeys, an Interval of Time being allowed for the Development of the Trypanosomes in the Fly.

No. of experiment.	Duration of treatment.	No. of doses.	No. of flies fed on patient.	No. of days flies fed on patient.	No. of days flies fed on monkey.	Result.	Remarks.
2103	7 days	2	60	6	50	—	Monkey remained healthy.
2168	7 „	2	63	6	50	—	„
2250	7 „	1	100	4	50	—	„
2034	30 „	4	100	3	50	+	<i>T. gambiense</i> appeared in blood.
2098	30 „	4	50	5	50	—	Monkey remained healthy.
2105	30 „	4	65	4	50	—	„
2189	30 „	4	60	7	50	—	„
2191	30 „	4	65	7	50	—	„
2244	2½ years	?	120	4	50	—	„
2242	Nil	Nil	85	4	50	—	„

Remarks.—In Table IV, Class C, 10 experiments are recorded. One of these was from an untreated case with large numbers of trypanosomes in the cervical glands, but none detectable in the blood.

The monkey was not infected by flies fed upon this patient, and so the flies were not dissected.

Of the 9 experiments from treated cases, Class C, three were from two patients who had been under treatment for one week, of whom one had been given a single dose of soamin 2 grammes, and HgCl₂ 0·04 gramme. The other patient had received two doses.

The experiments performed from these patients were negative as regards infection of both monkeys and flies.

Three patients had been under treatment for one month. Each of these patients had been given injections of soamin and perchloride of mercury, amounting to 2 grammes of the former drug and 0·08 gramme of the latter. One of these experiments was positive, both as regards infecting the flies and transmitting the disease to monkeys.

Seventy-five flies were dissected from the positive experiment, 2034. Of these, four flies were found to be infected with *Trypanosoma gambiense* on the 28th, 39th, 40th, and 46th day respectively after their last infected feed. The four flies found to be infected with trypanosomes were injected into a susceptible animal, which subsequently developed Sleeping Sickness.

It is obvious that the results obtained from these experiments, though giving us some information, are insufficient to warrant a decisive answer to the questions before us.

With regard to the first query: Can treatment of Sleeping Sickness patients by the drugs named influence the infectivity of the fly? Omitting the mechanical transmission experiments, we may say that out of the 35 experiments only one produced a positive result, *i.e.* flies were infected and the disease transmitted from a Sleeping Sickness patient under treatment to a normal monkey. The case referred to above will also entitle us to express an opinion as to whether one or more doses of a certain trypanocidal

drug can render a patient non-infective to the fly. It will be seen that this case had been under treatment for one month, and had been injected with four doses of trypanocidal drugs. The tsetse flies were infected 25 days after the last of the four injections had been administered.

Therefore, it may be said that to treat Sleeping Sickness patients with injections of soamin and perchloride of mercury, as specified, does not necessarily cause their blood to be incapable of infecting *Glossina palpalis* with *Trypanosoma gambiense*, and that flies so infected can transmit the disease to monkeys.

The percentage of flies infected from untreated cases was not ascertained, as only 190 flies were dissected, at various intervals, after feeding on their patients, and none were found infected.

A total of 857 flies were dissected, at different periods, after having fed upon treated cases, and four of these were found to be infected, *i.e.* a percentage of 0.46. These four flies all came from a cage containing 100 *Glossina palpalis* which had been fed on three occasions upon the only treated case that proved infective to the flies, *vide* Table IV, Experiment 2034. This patient therefore infected 4 per cent. of flies—an interesting and important fact.

It was hoped that patients under the influence of trypanocidal drugs would be incapable of infecting tsetse flies. Unfortunately, this experiment (2034) is sufficient to show that Sleeping Sickness patients under treatment with arsenical compounds, etc., are not always innocuous to the fly, and should not be allowed their freedom to wander about the country during intervals of comparative good health, but must be kept completely and permanently isolated from all possible contact with the fly.

Conclusions.

1. *Glossina palpalis* fed on natives suffering from Sleeping Sickness, and untreated by drugs, may become infected and be capable of transferring the disease to healthy animals.

2. *Glossina palpalis* fed on natives suffering from Sleeping Sickness, and treated by arsenic and other drugs, may also become infected and be capable of transferring the disease to healthy animals.



